4 Estimation of Nicotine and Tobacco Specific Nitrosamines (TSNA) in Saliva After Nicotine Infusion and After Smoking

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The contribution of salivary glands to the excretion of nicotine and TSNA which may derive from nicotine was investigated in two studies. In the first study, four healthy male cigarette smokers received three nicotine infusions (2  $\mu$ g·min<sup>-1</sup>·kg<sup>-1</sup> for 10 min each) with an interval of 50 min between infusion 1 and 2, and an interval of 15 min between infusion 2 and 3. Nicotine and its main metabolite cotinine were measured in serum and in saliva from the parotid gland, the submandibular gland and in mixed saliva. In the second study, four healthy male cigarette smokers received one nicotine infusion as in study 1. After one hour they were asked to smoke four cigarettes within 50 minutes and a further four cigarettes two hours later. Nicotine and cotinine were monitored in serum and in pooled saliva from the parotid gland over the whole time. Saliva specimens were sampled to determine tobacco-specific nitrosamines.

Ten to twenty minutes after the beginning of the nicotine infusion nicotine concentration was about 20 times higher in saliva from the submandibular gland and about 60 times higher in saliva from the parotid gland as compared to serum levels. Intermediate values were obtained in mixed saliva. After smoking nicotine values in pooled saliva from the parotid gland were about 10 times higher than those in serum. Nicotine concentration in saliva reached peak values between 600 and 2000 ng/ml after infusion and mean values in the pooled samples between 150 and 500 ng/ml after smoking. Cotinine values in saliva are slightly higher than those in serum, but the differences are marginal. TSNA could neither be detected after nicotine infusion nor after smoking.

The increase in salivary nicotine is due to the fact that saliva is more acidic than is serum. As in the renal handling process, nicotine is rapidly protonated in the saliva and the salt is not able to cross the membrane back to blood. A comparable increase in cotinine and TSNA in saliva should not be expected since these substances are less alkaline than nicotine.